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Investigation on nanoparticle distribution for thermal ablation of a tumour subjected to nanoparticle assisted thermal therapy

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ABSTRACT

This study investigates the effect of the distribution of nanoparticles delivered to a skin tumour for the thermal ablation conditions attained during thermal therapy. Ultimate aim is to define a distribution of nanoparticles as well as a combination of other therapeutic parameters to attain thermal ablation temperatures (50–60 °C) within whole of the tumour region. Three different cases of nanoparticle distributions are analysed under controlled conditions for all other parameters viz. irradiation intensity and duration, and volume fraction of nanoparticles. Results show that distribution of nanoparticles into only the periphery of tumour resulted in desired thermal ablation temperature in whole of tumour. For the tumour size considered in this study, an irradiation intensity of 1.25 W/cm^2 for duration of 300 s and a nanoparticle volume fraction of 0.001% was optimal to attain a temperature of $\geq$53 °C within the whole tumour region. It is concluded that distribution of nanoparticles in peripheral region of tumour, along with a controlled combination of other parameters, seems favourable and provides a promising pathway for thermal ablation of a tumour subjected to nanoparticle assisted thermal therapy.

1. Introduction

Thermal therapy in form of hyperthermia or thermal ablation is well-known technique for cancer treatment as standalone or in combination with other modalities (Vander, 2002; Dewhirst et al., 2013; Wust et al., 2002). Thermal ablation techniques generally involve absorbing electromagnetic waves inside the tumour region to generate the required thermal energy. Since tumours are surrounded by healthy tissue, selectivity during thermal ablation can potentially be managed through suitable nanoparticles delivered to a tumour (Hirsch et al., 2003; Maltzahn et al., 2009). Here nanoparticles are used as the energy absorbers (through optical interaction), and this technique is referred to as nanoparticle assisted thermal therapy. In this therapy, a tumour embedded with nanoparticles is irradiated suitably within the so-called 'therapeutic window' (600–1300 nm) (Mobley and Vo-Dinh, 2003).

Since nanoparticles act as source of heat, their spatial distribution and concentration in and around the tumour region govern the spatial extent of thermal ablation in the region. Various methods of particle delivery result in varying distributions of nanoparticles within the tumour (Dreher et al., 2006; Goodman et al., 2008; Su et al., 2010). Unfortunately, any real attempt at intra-tumour/local injection of nanoparticles to the tumour results in non-uniform spatial distributions. In fact, an ideal, perfectly uniform distribution of particles which only resides in the tumour region is likely impossible to achieve by any means. Most published studies in this field assumed a uniform distribution of nanoparticles within a tumour (Feng et al., 2009; Terentyuk et al., 2009; Xu et al., 2011). To some extent, this issue of nanoparticle distribution has been touched upon for the gold nanoshells (Dombrovsky et al., 2012). However, this remains a major, under developed issue since the distribution of injected nanoparticles critically governs the spatiotemporal temperature field within a tumour. This study addresses and quantifies the extent of this issue.

This study expands upon the previous work, in the area of gold nanorod assisted thermal therapy, of the co-authors (Soni et al., 2013). This study highlights the role of nanoparticle distribution on the spatiotemporal temperature fields within a two dimensional skin tumour. Three cases of nanoparticle distribution are considered – (a) uniformly distributed throughout the tumour

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region, (b) accumulated within tumour core, and (c) accumulated at the tumour periphery. For each case, the effect of other key parameters like irradiation intensity, irradiation duration and volume fraction of nanoparticles are also evaluated. Finally, a distribution of nanoparticles and an appropriate selection of other parameters are proposed to attain the desired temperature for thermal ablation within whole of tumour region.

2. Theory and methods

2.1. Skin tumour and distribution of nanoparticles:

A typical skin tumour was approximated in two dimensional cylindrical coordinates. The tumour region is 20 mm in diameter and has a 5 mm depth. A cylindrical tumour has been considered in earlier studies (Dombrovsky et al., 2012; Zhang et al., 2008). It is surrounded by healthy tissue of diameter 40 mm and a depth 10 mm, as shown in Fig. 1. These tumour dimensions correspond to high risk skin cancers (Breslow, 1970; Samarasinghe and Madan, 2012).

The nanoparticles are usually delivered either by intravenously or through an intra-tumour/local injection at the tumour site (Hirsch et al., 2003; Maltzahn et al., 2009). Considering the complex tumour biology and physiology involved, it is not possible to deliver nanoparticles uniformly to the whole of tumour through intravenous delivery (Kuszyk et al., 2001; Jain and Stylianopoulos, 2010). For tumours which are near the surface, it is possible to inject nanoparticles directly into the treatment area. In this case, nanoparticles accumulate in a restricted area in and around the injection site. Depending upon the nanoparticle delivery method, three cases of spatial distribution of nanoparticles i.e. gold nanorods (GNR), within the tumour, were considered. These are shown in Fig. 2.

2.1.1. Case I

Since nanoparticles act as source of heat, the first case selected was based on the commonly used uniform distribution of nanoparticles within the tumour. This corresponds to an ideal heating case; however, it is difficult to have uniform distribution of injected nanoparticles within the tumour. This was considered as a baseline case for this study and is shown pictorially in Fig. 2(a). This type of distribution is referred to as *Case I* throughout this paper. The GNR are embedded in tumour region of 10 mm radius and 5 mm depth.

2.1.2. Case II

Case II was selected to represent the method of delivering nanoparticles through injection to the tumour site (Hirsch et al., 2003). Locally injected nanoparticles are confined to a region around the injection site (Su et al., 2010). Also, there is gradient in concentration/volume fraction (f_v) of nanoparticles from the injection site. This was incorporated in the present study through a function of exponential form $f_v(R) = f_v \exp(-0.1R^2)$ for calculation of optical coefficients of GNR as a function of tumour radius R. In this case, GNR were considered to be confined to approximately half the region of tumour (radius 5 mm and depth 2.5 mm) as

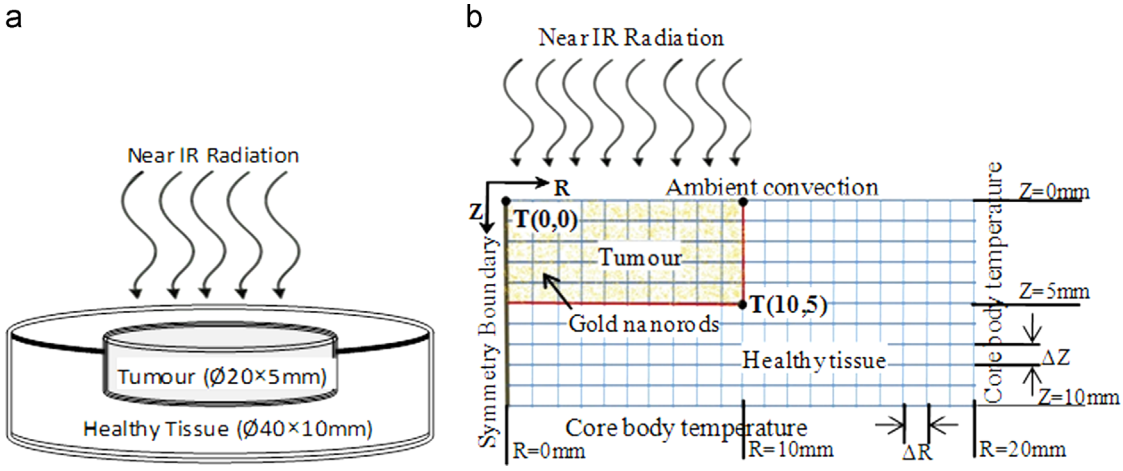

Fig. 1. Schematic representing (a) the tumour region surrounded by healthy skin tissue and (b) symmetric R–Z cross-section of the tissue. The tumour is surrounded by healthy tissue of 5 mm thickness at the bottom and a 10 mm thick annulus. The symbols R and Z represent radius and depth of tissue respectively. Corresponding ΔR and ΔZ represent dimensions of a nodal region. T represent temperature at spatial location R, Z.

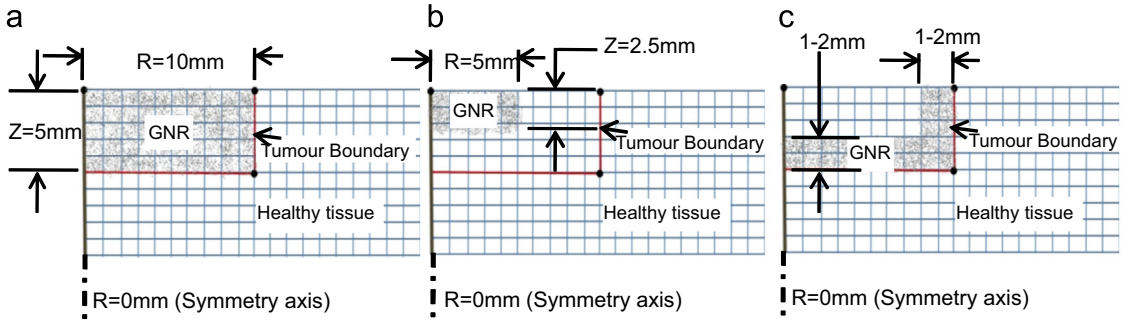

Fig. 2. Three cases of spatial distribution of nanoparticles injected to the tumour. (a) Ideal case – nanoparticles distributed throughout the tumour, (b) intratumour injection – nanoparticles accumulated in the core of tumour and (c) intravenous injection – nanoparticles distributed in periphery of tumour. GNR represents 'gold nanorods' taken as nanoparticles.